A Ground-Based Analog for CNS Exposure to Space Radiation: A System for Integrating Microbeam Technology and Neuronal Culture

Completed Technology Project (2017 - 2021)

Project Introduction

Problem Statement: The connection between radiation-induced neuronal damage and deficits in behavior and cellular function is still largely unknown. Previous studies on the effects of space-like radiation have lacked the technology to selectively irradiate individual cells in culture, much less individual cellular structures. Thus there is currently no way to observe how individual neurons respond to radiation-induced damage of specific cellular structures, which is critical to building the mechanistic link between radiation damage and physiological changes. Overall Goal: This project aims to develop a system utilizing particle microbeam technology and neuronal cell culture that can serve as a ground-based analog to neuron exposure to space radiation. This neuron-microbeam system will be used to investigate the molecular and cellular effects of high-energy particle radiation on the central nervous system. Background: Space radiation poses one of the least understood and least mitigated risks to humans traveling outside the protection of Earth's magnetic field. Previous radiation biology research has primarily focused on DNA damage and the resulting carcinogenesis risk, and this work has been largely concerned with low linear energy transfer (LET) ionizing radiation such as gamma rays and X-rays. However, space radiation includes a variety of high atomic number, high-energy (HZE) ions that transfer large amounts of energy when traversing biological materials. A Mars trip would expose astronauts to a total of about 0.2 Gy of HZE ions. This dose is relatively small for low LET radiation, but HZE ions with a high LET can inflict significant biological damage even at this low dose. The long-standing radiation biology theory that DNA is the primary radiosensitive target in cells may not hold true for the central nervous system (CNS) in the low-fluence, high-energy charged particle radiation environment of space. Because much of the CNS consists of volumes containing mostly cellular processes and relatively few cell bodies, it is plausible that in low dose and dose rate conditions, only a small fraction of cells traversed by a charged particle will suffer damage to the nucleus. Thus the observed radiation-induced deficits are likely caused by the traversal of a particle through some extra-nuclear component of the cell. Research Plan: The early stages of this project will focus on developing a cell culture method for neurons that fits the tight constraints of the microbeam system. The new culture method will be evaluated by its ability to replicate previously observed changes in dendritic spine morphology and concentrations of cytoskeletal proteins. The latter stages of this project will focus on integrating this cell culture method with the particle microbeam at Columbia University's Radiological Research Accelerator Facility. A custom imaging and targeting protocol will be developed using fluorescent reporters and the microbeam facility's targeting system to selectively irradiate subcellular structures of individual neurons in neuronal cultures. Aim 1: Development of a neuronal culture procedure compatible with the particle microbeam system Aim 2: Integration of microbeam targeting system and neuronal culture. Aim 3: Validation of neuron-microbeam system via selective irradiation of neuronal dendrites Impact: This project aims to create the technological capacity to

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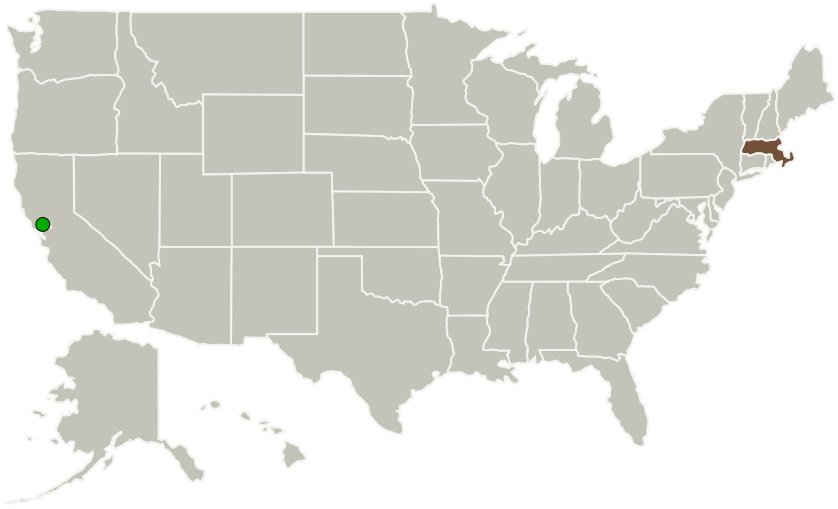
investigate cellular responses to specific, subcellular radiation targets for the purpose of building the mechanistic link between radiation damage and deficits in health and performance. Having this capability will help address the knowledge gaps related to acute central nervous system exposure to space radiation. This work can also be adapted to address the radiation exposure of other tissue types and has the potential to impact earth-side endeavors, namely the treatment of brain tumors with high-energy charged particle radiation.

Anticipated Benefits

This project aims to create the technological capacity to investigate cellular responses to specific, subcellular radiation targets for the purpose of building the mechanistic link between radiation damage and deficits in health and performance. Having this capability will help address the knowledge gaps related to acute central nervous system exposure to space radiation. This work can also be adapted to address the radiation exposure of other tissue types and has the potential to impact earth-side endeavors, namely the treatment of brain tumors with high-energy charged particle radiation.

Primary U.S. Work Locations and Key Partners



Organizational Responsibility

Responsible Mission Directorate:

Space Technology Mission Directorate (STMD)

Lead Organization:

Massachusetts Institute of Technology (MIT)

Responsible Program:

Space Technology Research Grants

Project Management

Program Director:

Claudia M Meyer

Program Manager:

Hung D Nguyen

Principal Investigator:

Julie Greenberg

Co-Investigator:

Robert G Hinshaw

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Organizations Performing Work	Role	Type	Location
Massachusetts Institute of Technology(MIT)	Lead Organization	Academia	Cambridge, Massachusetts
Ames Research Center(ARC)	Supporting Organization	NASA Center	Moffett Field, California

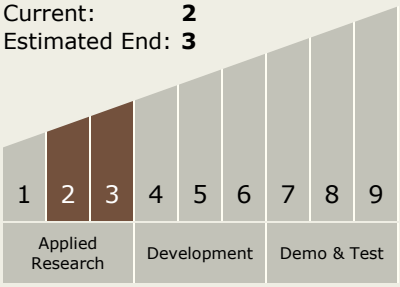
Primary U.S. Work Locations
Massachusetts

Project Website:

https://www.nasa.gov/strg#.VQb6T0jJzyE

Technology Maturity (TRL)

Start: **2**
Current: **2**
Estimated End: **3**



Technology Areas

Primary:

- TX06 Human Health, Life Support, and Habitation Systems
  - TX06.5 Radiation
    - TX06.5.1 Radiation Transport and Risk Modeling

Target Destination

Earth